Hypoparathyroidism is characterized by low calcium and low parathyroid hormone (PTH) levels. Hyperphosphatemia, hypercalciuria, and reduced active vitamin D are associated with hypoparathyroidism.[1] The main clinical features of the disease are hypocalcemic symptoms such as perioral numbness, paresthesia, and carpopedal muscle spasms. In addition, some severe and potentially life-threatening complications such as laryngeal spasms, tetany and seizures may occur during the course of hypoparathyroidism. The most common cause of hypoparathyroidism is accidental damage to the parathyroid glands during thyroid surgery.[2]

There are no formal guidelines for hypoparathyroidism management. In the acute setting, intravenous administration of calcium may be necessary. Based on current clinical evidence, the main goal of treatment is to improve the symptoms of hypocalcemia, to keep the serum calcium within the low normal range, and to avoid hypercalcemia and hypercalciuria, regardless of etiology by providing standard hypoparathyroidism treatment with oral calcium and vitamin D supplements at different doses.[3] In 2015, the United States Food and Drug Administration (FDA) approved the use of recombinant human PTH (1-84) in treating patients with classical treatment-resistant hypoparathyroidism.[4,5] It is expected that the PTH analogues would be mainstay for the treatment for regaining normal physiology. Although teriparatide, a recombinant human PTH (1-34), is widely used in the treatment of osteoporosis, there is a limited number of literature data on its use for hypoparathyroidism. A study comparing parenteral teriparatide with classical oral treatment showed that parenteral therapy was more effective in reducing hypercalciuria and improving quality of life.[6]

In addition, when once-daily regimen was compared with twice-daily regimen, the latter was found to be more effective.[7] The long-term use of

**ABSTRACT**

Hypoparathyroidism usually responds to oral active vitamin D and calcium, but, although rare, some patients do not respond to this treatment. A 47-year-old Caucasian female presented to our medical unit with classical oral treatment-resistant hypocalcemia after thyroidectomy. Teriparatide was infused through the insulin pump with dosage set to 1 unit which equals to 2.5 µg of teriparatide.

In conclusion, intermittent subcutaneous infusion of teriparatide using an insulin pump is a safe and effective treatment modality to ensure normocalcemic conditions in patients with classical treatment-resistant hypoparathyroidism.

**Keywords:** Hypoparathyroidism; pump infusion; teriparatide.

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Alternative treatment of resistant hypoparathyroidism by intermittent infusion of teriparatide using an insulin pump

Teriparatide was also shown to be safe and effective. Moreover, it was observed that, compared to single-dose subcutaneous teriparatide injection, continuous infusion of teriparatide via an insulin pump was more effective. In another study, Puig-Domingo et al. succeeded to treat the treatment-resistant hypoparathyroidism through PTH in short-interval pulse-type to mimic physiological PTH release.

To the best of our knowledge, this is the first case in Turkey in whom teriparatide was administered for classical treatment-resistant hypoparathyroidism using an insulin pump and succeeded in achieving normocalcemia.

CASE REPORT

A 47-year-old Caucasian female patient presented with paresthesia and carpopedal spasm. The patient underwent total thyroidectomy due to multinodular goitre two years ago. Thereafter, the patient developed postoperative hypoparathyroidism and was hospitalized several times in the emergency setting and treated for correcting hypocalcemia. She was admitted to the Endocrinology Department due to resistant hypoparathyroidism. On admission, her physical examination results were normal, except for thyroidectomy scars and carpopedal spasm. The laboratory values were as follows: PTH 8.6 (15-65) pg/dL, serum calcium 6.4 (8.5-10.5) mg/dL, phosphorus 5.4 (2.7-4.8) mg/dL, and albumin 3.3 (4-5) mg/dL. Although she was on regular medication of calcitriol 6 µg/day, elemental calcium 12 g/day, oral 1,25-OH vitamin D and oral magnesium, hypocalcemia was persistent. Normocalcemia was achieved by parenteral calcium administration in our clinic. Celiac panel and small bowel biopsy were carried out for exclusion of malabsorption syndrome and were found to be negative. Since hypercalciuria (960 mg/day) was detected, the patient was administered thiazide diuretic. Parenteral active vitamin D was administered to the patient rather than oral vitamin D therapy. However, hypocalcemia was unable to be corrected. Therefore, teriparatide was administered. We initiated once daily 20 µg subcutaneous injection of recombinant human PTH (1-34)

![Figure 1. Teriparatide through an insulin pump.](image-url)

![Figure 2. Treatment methods and calcium level. Sc: Subcutaneous.](image-url)
(Teriparatide; Lilly France S.A.S, Forsteo®, Fegersheim, France). Although the dose was titrated up to 60 µg/day in three equal doses, hypocalcemia still remained uncorrected. Therefore, continuous teriparatide infusion using an insulin pump was suggested. The insulin pump was calibrated such that 1 unit (Minimed Medtronic) equals 2.5 µg of teriparatide. Normocalcemia was achieved with continuous dose infusion (1 unit/hour, totally 60 µg teriparatide). However, during follow-up, the patient experienced hypercalcemia due to this treatment. Due to the presence of hypercalcemia, the dose of teriparatide infusion was adjusted to mimic physiological PTH release as 1.1 unit for one-hour infusion and one-hour off (totally 33 µg/day teriparatide) and normocalcemia was achieved (Figure 1). The level of 1,25-dihydroxy vitamin D level was normal during teriparatide treatment after which the patient’s calcium levels improved. Oral calcium and active vitamin D requirements decreased. After several admissions to the hospital for two years, the patient was eventually discharged with this treatment. The patient did not need any additional therapy for the next seven months after discharge. The patient has been still waiting for parathyroid transplantation under this therapy.

**DISCUSSION**

Hypoparathyroidism, which does not respond to active vitamin D, is a very rare condition. The success rate of parathyroid transplantation is low worldwide, as most attempts have resulted in transplant rejection.[10] Therefore, it seems reasonable to use PTH analogues in such patients.

Previous use of teriparatide has focused more on non-normocalcemic effects.[11] There are also several publications on the use of PTH analogues, since its approval by the FDA in recent years.[5,12] Studies on PTH (1-34) have shown that subcutaneous administration is more effective than classical oral treatment. Meanwhile, better results were obtained with the continuous infusion via insulin pump than with the subcutaneous injection. However, no resistant hypocalcemic patients were reported in these studies.[13] Andrysiak-Mamos et al.[14] found that three patients with postoperative resistance hypoparathyroidism were treated with subcutaneous 20 to 80 µg/day teriparatide successfully.[14] Diaz-Soto et al.[15] reported teriparatide infusion through a pump in a patient with hypoparathyroidism resistant to vitamin D treatment. Teriparatide was infused in five to seven impulse doses per hour. The treatment was observed to be effective and safe for five years. Saraff et al.[16] provided normocalcemia in four patients through subcutaneous teriparatide infusion, and observed no side effects for the first year.[16] In our case, we also achieved successful results with intermittent infusion.

In conclusion, we believe that teriparatide, a PTH analogue, provides normocalcemia with intermittent subcutaneous infusion in patients with classical treatment-resistant hypoparathyroidism. Since in the literature review, no case in whom normocalcemia is able to be achieved with intermittent constant one hourly infusion of teriparatide is available, this is the first case in whom normocalcemia was achieved by intermittent infusion of PTH 1-34 in Turkey.

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